composed of modified oligonucleotides (*e.g.*, for improved stability, targeting, etc.), and should be delivered to cells which express the GLUTX *in vivo*. A preferred method of delivery involves using a DNA construct "encoding" the ribozyme under the control of a strong constitutive *pol* III or *pol* II promoter, so that transfected cells will produce sufficient quantities of the ribozyme to destroy endogenous GLUTX messages and inhibit translation. Because ribozymes, unlike antisense molecules, are catalytic, a lower intracellular concentration is required for efficiency.

## VII. Peptide Nucleic Acids

Nucleic acid molecules encoding GLUTX (or a fragment thereof) can be modified at the base moiety, sugar moiety, or phosphate backbone to improve, for example, the stability or solubility of the molecule or its ability to hybridize with other nucleic acid molecules. For example, the deoxyribose phosphate backbone of the nucleic acid can be modified to generate peptide nucleic acids (see Hyrup *et al.*, *Bioorganic Med. Chem.* 4:5-23 (1996). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, for example, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.*, *supra*; Perry-O'Keefe *et al. Proc. Natl. Acad. Sci. USA* 93:14670-14675 (1996).

PNAs of GLUTX can be used in therapeutic and diagnostic applications. For example, PNAs can be used as

antisense or antigene agents for sequence-specific modulation of gene expression by, for example, inducing transcription or translation arrest or inhibiting replication. PNAs of GLUTX can also be used, for example, in the analysis of single base pair mutations in a gene by, for example, PNA-directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, for example, S1 nucleases (Hyrup *et al.*, *supra*); or as probes or primers for DNA sequence and hybridization (Hyrup *et al.*, *supra*; Perry-O'Keefe, *supra*).

In other embodiments, PNAs of GLUTX can be modified, for example, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to the PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of GLUTX can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, for example, RNAse H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup *et al.*, *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *supra*, and Finn *et al.*, *Nucl. Acids Res.* 24:3357-3363 (1996). For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag *et al.*, *Nucl. Acids Res.* 17:5973-5988, 1989). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule

with a 5′ PNA segment and a 3′ DNA segment (Finn *et al.*, *supra*). Alternatively, chimeric molecules can be synthesized with a 5′ DNA segment and a 3′ PNA segment (Peterser *et al.*, *Bioorganic Med. Chem. Lett.* 5:1119-11124 (1975).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, *Proc. Natl. Acad. Sci. USA* 86:6553-6556 (1989); Lemaitre *et al.*, *Proc. Natl. Acad. Sci. USA* 84:648-652 (1987); PCT Publication No. WO 88/09810, published December 15, 1988) or the blood-brain barrier (see, *e.g.*, PCT Publication No. WO 89/10134, published April 25, 1988). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, *e.g.*, Krol *et al.*, *BioTech.* 6:958-976 (1988)) or integrating agents (see, *e.g.*, Zon, *Pharm. Res.* 5:539-549 (1988)). To this end, the oligonucleotide may be conjugated to another molecule, for example, a peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent etc.

**VIII. Proteins that Associate with GLUTX**

The invention also features methods for identifying polypeptides that can associate with GLUTX, as well as the isolated interacting protein. Any method that is suitable for detecting protein-protein interactions can be employed to detect polypeptides that associate with GLUTX, whether these polypeptides associate with the transmembrane, intracellular, or extracellular domains of GLUTX. Among the traditional methods that can be employed are co-immuno-precipitation, crosslinking, and co-purification through